

We claim:

1. A method for inducing a biological response in a biological system comprising one or more receptors which comprises the step of introducing into the biological system a multivalent ligand which comprises a plurality of signal recognition elements recognized by at least one of the receptors and bonded to a molecular scaffold.
2. The method of claim 1 wherein the biological system comprises a cell having one or more cell receptors to which at least one of the signal recognition elements bind.
3. The method of claim 2 wherein binding of the signal recognition element to the receptor induces an intracellular response and/or an intercellular response.
4. The method of claim 1 wherein the cell is a prokaryotic cell.
5. The method of claim 4 wherein the multivalent ligand modulates signal transduction mediated by a two component system.
6. The method of claim 5 wherein the biological response is chemotaxis.
7. The method of claim 6 wherein the signal recognition element is a saccharide and the multivalent ligand comprises a plurality of the saccharides that function as chemoattractants covalently attached to a molecular scaffold.
8. The method of claim 7 wherein the saccharide is glucose or galactose.
9. The method of claim 6 wherein the multivalent ligand enhances chemotaxis of the prokaryotic cell.
10. The method of claim 6 wherein the multivalent ligand inhibits chemotaxis of the prokaryotic cell.

11. The method of claim 5 wherein the biological response is the formation of a biofilm.
12. The method of claim 11 wherein the multivalent ligand inhibits biofilm formation.
- 5 13. The method of claim 11 wherein the multivalent ligand enhances biofilm formation.
14. The method of claim 5 wherein the biological response is nutrient uptake.
- 10 15. The method of claim 14 wherein the multivalent ligand prevents or inhibits nutrient uptake.
16. The method of claim 14 wherein the multivalent ligand enhances nutrient uptake.
17. The method of claim 2 wherein the cell is a eukaryotic cell.
- 15 18. The method of claim 17 wherein the multivalent ligand modulates signal transduction mediated by G-protein coupled receptors.
19. The method of claim 18 wherein signal transduction is mediated by receptors.
- 20 20. The method of claim 17 wherein the eukaryotic cell is an epithelial cell or an endothelial cell.
21. The method of claim 17 wherein the eukaryotic cell is a cell of the immune system.
- 25 22. The method of claim 21 wherein the eukaryotic cell is a lymphocyte or an leukocyte.
23. The method of claim 21 wherein the eukaryotic cell is a neutrophil.
- 30 24. The method of claim 23 wherein the response is chemotaxis.

25. The method of claim 24 wherein one or more of the signal recognition elements is a formylated peptide and wherein the multivalent ligand comprises a plurality of formylated peptides covalently bonded to a molecular scaffold.
- 5 26. The method of claim 25 wherein the multivalent ligand inhibits neutrophil chemotaxis.
27. The method of claim 25 wherein the multivalent ligand enhances neutrophil chemotaxis.
- 10 28. The method of claim 17 wherein the biological response is the release of an intracellular signal by the cell.
29. The method of claim 28 wherein the multivalent ligand initiates or enhances the release of the intracellular signal.
- 15 30. The method of claim 21 wherein the cell is a B-cell or a T-cell.
31. The method of claim 30 wherein the multivalent ligand comprises a signal recognition element that is an epitope foreign to the organism from which the B-cell or T-cell originates.
- 20 32. The method of claim 31 wherein the multivalent ligand further comprises a signal recognition element that binds to a cell surface receptor of a B-cell or a T-cell.
- 25 33. The method of claim 32 wherein the multivalent ligand functions to enhance immunogenicity of the foreign epitope.
34. The method of claim 30 wherein the multivalent ligand comprises a signal recognition element that is an epitope recognized as a self epitope by the B- cell or T-cell.
- 30 35. The method of claim 34 wherein the multivalent ligand further comprises a signal recognition element that binds to a cell surface receptor of a B-cell or a T-cell.

36. The method of claim 35 wherein the multivalent ligand functions to sensitize the cell to the self epitope.
- 5 37. The method of claim 36 wherein the epitope is an epitope that is characteristic of a cancer cell.
38. The method of claim 30 wherein the multivalent ligand comprises at least one signal recognition element that is a self epitope which is recognized as a foreign epitope by the B-cell or T-cell.
- 10 39. The method of claim 38 wherein the multivalent ligand further comprises a signal recognition element that binds to a cell surface receptor of a B-cell or a T-cell.
- 15 40. The method of claim 39 wherein the multivalent ligand functions to tolerize the cell to the self epitope that is recognized as a foreign epitope by the B-Cell or T-cell.
41. The method of claim 1 wherein the multivalent ligand reorganizes receptors on the surface of a cell to modulate the biological response.
- 20 42. The method of claim 41 wherein the relative positions of different receptors on the cell surface is changed to modulate the response.
43. The method of claim 42 wherein interactions between cell surface receptors are changed to modulate the response.
- 25 44. The method of claim 1 wherein the biological response is an immune response to an antigen or epitope that is foreign to the biological system.
- 30 45. The method of claim 44 wherein the multivalent ligand modifies the immune response the foreign antigen or epitope and wherein the multivalent ligand comprises a signal

recognition element that is an epitope or antigen that is recognized as foreign by the immune cell, cells or immune system that mediates the immune response.

46. The method of claim 1 wherein the biological response is an immune response to an antigen or epitope that is recognized as self by the biological system.

47. The method of claim 46 wherein the multivalent ligand modifies the immune response to an antigen or epitope that is recognized as self and wherein the multivalent ligand comprises a signal recognition element that is an epitope or antigen that is recognized as self by the immune cell, cells or immune system.

48. The method of claim 1 wherein the biological system is an animal.

49. The method of claim 1 wherein the biological system is a mammal.

50. The method of claim 1 wherein the biological system is a human.

51. A method for treating a bacterial infection which comprises the step of administering a therapeutically effective amount of a multivalent ligand to an individual having a bacterial infection wherein the multivalent ligand comprises a plurality of signal recognition elements that are chemoattractant signals covalently bonded to a molecular scaffold.

52. A pharmaceutical composition for treating a bacterial infection which comprises an amount of a multivalent ligand effective for inhibiting the chemotaxis response in the bacterium, wherein the multivalent ligand comprises a plurality of signal recognition elements that are chemoattractant signals covalently bonded to a molecular scaffold, and a pharmaceutically acceptable carrier.

53. A method for modulating the chemotaxis response of a eukaryotic cell which comprises the step of contacting the eukaryotic cell with a multivalent ligand which comprises a plurality of signal recognition elements that are chemoattractants of the eukaryotic cell.
- 5 54. A method for treating an infection of a eukaryotic pathogen or parasite which comprises the step of administering a therapeutically effective amount of a multivalent ligand to an individual having an infection wherein the multivalent ligand comprises a plurality of signal recognition elements that are chemoattractants of the pathogen or parasite covalently bonded to a molecular scaffold.
- 10 55. A pharmaceutical composition for treating an infection of a eukaryotic pathogen or parasite which comprises an amount of a multivalent ligand effective for inhibiting the chemotaxis response in the pathogen or parasite, the multivalent ligand comprising a plurality of signal recognition elements that are chemoattractants covalently bonded to a
- 15 molecular scaffold, and a pharmaceutically acceptable carrier.
56. The method of claim 1 wherein the response is cell migration, cell adhesion, or the formation of cell to cell junctions.
- 20 57. The method of claim 56 wherein the multivalent ligand inhibits cell migration, cell adhesion, or the formation of cell to cell junctions.
58. The method of claim 57 wherein the cell is a cancer cell in an animal.
- 25 59. The method of claim 1 wherein the multivalent ligand further comprises one or more recognition elements, one or more functional elements or both.
60. The method of claim 59 wherein one or more of the recognition elements binds to a protein.
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61. The method of claim 59 wherein one or more of the functional elements is a label or a reporter group.
- 5 62. The method of claim 1 wherein one or more of the signal recognition elements is selected from the group consisting of an amino acid, a peptide, a protein, a derivatized peptide, a monosaccharide, a disaccharide, a polysaccharide, a nucleic acid, a cell nutrient, an epitope, an antigenic determinant, a hapten, or a cell surface receptor.
- 10 63. The method of claim 1 wherein one or more of the signal recognition elements is a saccharide or a derivatized saccharide.
64. The method of claim 1 wherein one or more of the signal recognition elements is a peptide or a derivatized peptide.
- 15 65. The method of claim 1 wherein one or more of the signal recognition elements is a protein.
66. The method of claim 1 wherein one or more of the signal recognition elements is an N-formyl peptide.
- 20 67. The method of claim 1 wherein one or more of the signal recognition elements is an epitope.
68. The method of claim 1 wherein the multivalent ligand comprises a defined number of signal recognition elements.
- 25 69. The method of claim 1 wherein the multivalent ligand comprises 2 to about 10 signal recognition elements.
- 30 70. The method of claim 1 wherein the multivalent ligand comprises about 10 to 25 signal recognition elements .

71. The method of claim 1 wherein the multivalent ligand comprises about 25 or more signal recognition elements .

5 72. The method of claim 1 wherein the multivalent ligand comprises about 50 or more signal recognition elements.

73. The method of claim 1 wherein the multivalent ligand comprises about 100 or more signal recognition elements.

10 74. The method of claim 1 wherein the signal recognition elements are covalently bonded to the molecular scaffold.

15 75. The method of claim 1 wherein the signal recognition elements are noncovalently bonded to the molecular scaffold.

76. The method of claim 75 wherein the multivalent ligand further comprises a plurality of recognition elements covalently bonded to the scaffold wherein the signal recognition elements are in turn noncovalently bonded to one or more recognition elements.

20 77. The method of claim 76 wherein the recognition elements are saccharides and the signal recognition elements are peptides which bind noncovalently to the saccharides.

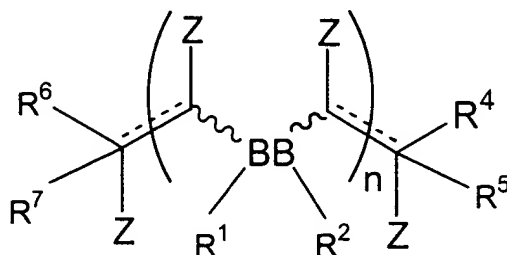
78. The method of claim 77 wherein the signal recognition elements are lectins.

25 79. The method of claim 78 wherein the lectins are concanavalin A.

80. The method of claim 1 wherein the molecular scaffold is selected from the group consisting of a polyacrylamide, a polyester, a polyether, a polymethacrylate, a polyol, and a polyamino acid.

81. The method of claim 1 wherein the molecular scaffold is a ROMP scaffold.

82. The method of claim 1 wherein the multivalent ligand has the structure:



wherein:

n is an integer that is 2 or more which represents the number of repeating units within the parentheses in the ligand;

the dashed lines indicate optional double bonds;

"BB" represents the backbone repeating unit, which may be cyclic or acyclic, and may be the same or different in a random or block arrangement, the wavy lines indicating that a BB unit may be in either a cis or trans configuration in the ligand backbone;

each R¹ and R², independently of other R¹ and R² in the ligand, can be H or an organic group, a recognition element -L²-RE, a functional element -L³-FE or a signal recognition element -L¹-SRE or both of R¹ and R² can be the -L¹-SRE group;

wherein L¹⁻³, independently, represent optional linker groups which may be the same or different in different repeating units;

R⁴ and R⁵ are H, or an organic group;

R⁶ and R⁷ are H, an organic group or an end-group; and

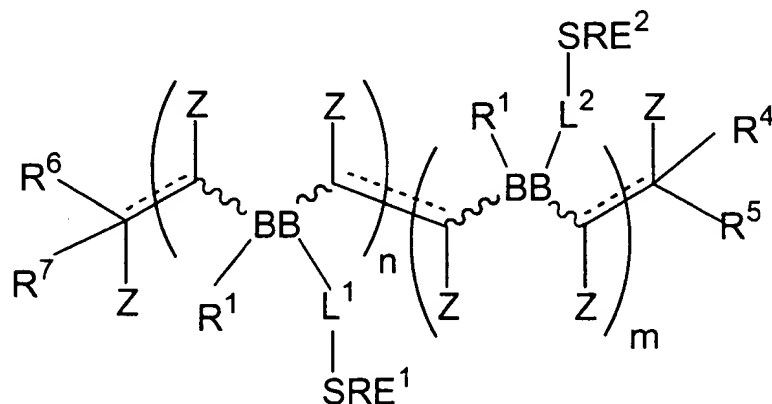
Z, independently of other Z in the ligand, is H, OH, OR⁸, SH, a halide (F, Br, Cl, I), NH₂ or N(R⁸)₂, where R⁸ is H or an organic group or Z is absent when the optional double bond is present.

83. The method of claim 82 wherein SRE is a peptide or a derivatized peptide.

84. The method of claim 83 wherein SRE is an N-formyl peptide.

85. The method of claim 82 wherein SRE is a chemoattractant.

86. The method of claim 82 wherein SRE is an epitope.
87. The method of claims 82 wherein at least one of SRE is an epitope and at least one other SRE binds to a cell surface receptor of an immune cell.
88. The method of claim 87 wherein the at least one other SRE binds to a cell surface receptor of a B-cell or a T-cell.
89. The method of claim 82 wherein at least one R^1 or R^2 is an $-L^3$ -FE group which is a detectable label or a reporter group.
90. The method of claim 82 wherein at least one R^1 or R^2 is an $-L^2$ -RE group.
91. The method of claim 82 wherein the multivalent ligand has the structure:



wherein:

$m + n$ is 2 or more;

dashed lines indicate the presence of optional double bonds;

“BB” represents the backbone repeating unit, which may be cyclic or acyclic, and may be the same or different in a random or block arrangement and wavy lines indicate that the BB unit may be in a cis or trans configuration in the backbone of the repeating unit;

each R^1 , independent of other R^1 in the ligand, can be H or an organic group;

L^1 and L^2 , which may be the same or different, represent optional linker groups;

SRE¹ and SRE² represent two different signal groups;

R⁴ and R⁵ are H, an organic group or an end-group;

R⁶ and R⁷ are H, an organic group or an end-group; and

Z, independently of other Z in the polymer, is H, OH, OR⁸, SH, a halide (F, Br, Cl, I),

NH₂ or N(R⁸)₂ where R⁸ is H or an organic group or Z is absent when a double bond is present.

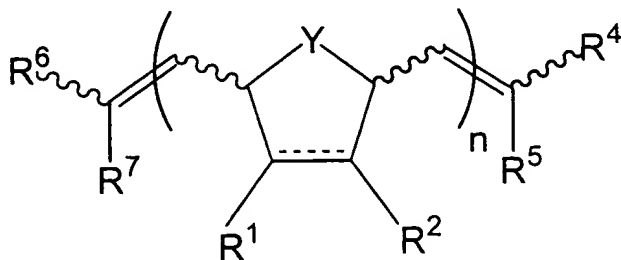
92. The method of claim 91 wherein one or both of SRE¹ and SRE² are peptides or derivatized peptides.

93. The method of claim 91 wherein one or both of SRE¹ or SRE² are saccharides or derivatized saccharides.

94. The method of claim 91 wherein one or both of SRE¹ or SRE² are epitopes.

95. The method of claim 91 wherein one of SRE¹ or SRE² is an epitope and the other of SRE¹ or SRE² binds to a cell surface receptor of an immune cell.

96. A multivalent ligand having the structure:



wherein:

n is an integer that is 2 or more that represents the number of repeating units within the parentheses in the ligand; the dashed line indicates an optional double bond

each Y, independent of other Y in the ligand, is an -O-, a -S-, an -NR⁸, or a -CH₂- group,

where R⁸ is H or an organic group;

each R^1 and R^2 , independent of other R^1 and R^2 in the ligand, can be H, an organic group, a signal recognition element $-L^1$ -SRE, a recognition element $-L^2$ -RE or a functional element $-L^3$ -FE, wherein at least one of the R^1 and R^2 groups in the ligand is $-L^3$ -SRE;

wherein L^{1-3} represent optional linker groups;

R^4 and R^5 are H, an organic group or an end-group; and

R^6 and R^7 are H, an organic group or an end-group.

97. The multivalent ligand of claim 96 wherein one of the R^1 or R^2 groups in each repeating unit of the ligand is $-L^1$ -SRE.

98. The multivalent ligand of claim 96 wherein at least one of the R^1 or R^2 groups in the ligand is $-L^2$ -RE .

99. The multivalent ligand of claim 96 wherein at least one of the R^1 or R^2 groups in the ligand is $-L^2$ -FE .

100. The multivalent ligand of claim 99 wherein the FE in the at least one $-L^2$ -FE group in the ligand is a detectible label or a reported group.

101. The multivalent ligand of claim 99 wherein the FE in the at least one $-L^2$ -FE group in the ligand is an enzyme.

102. The multivalent ligand of claim 96 wherein at least one of SRE is a peptide or a derivatized peptide.

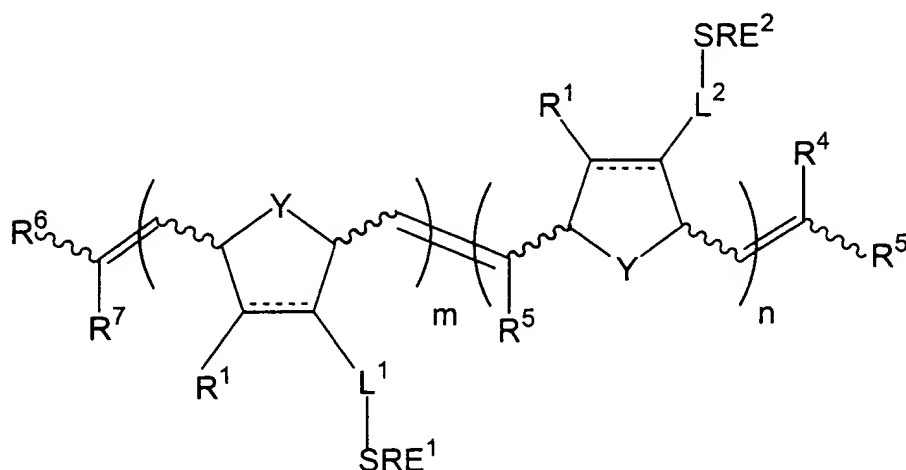
103. The multivalent ligand of claim 102 wherein at least one of SRE is an N-formyl peptide.

104. The multivalent ligand of claim 96 wherein at least one of SRE is an epitope.

105. The multivalent ligand of claim 104 wherein at least one of SRE binds to a cell surface receptor of an immune cell.

106. The multivalent ligand of claim 104 wherein at least one of SRE binds to a cell surface receptor of a B cell or a T cell.

107. The multivalent ligand of claim 96 having the structure:



wherein:

m + n is an integer of 2 or more and each integer represents the number of repeating units in the parentheses;

each Y, independent of other Y in the ligand, is -O-, -S-, -NR⁸-, or -CH₂-;

R¹ can be H, an organic group, a -L²-RE group or an -L³-FE group;

L¹ and L², which may be the same or different, represent optional linker groups;

SRE¹ and SRE² represent two different signal recognition elements;

R⁴ and R⁵ are H, an organic group or an end-group; and

R⁶ and R⁷ are H, an organic group or an end-group.

108. The multivalent ligand of claim 107 wherein one of SRE¹ or SRE² is a peptide or a derivatized peptide and the other of SRE¹ or SRE² is a saccharide.

109. The multivalent ligand of claim 108 wherein SRE¹ or SRE² are two different peptides or derivatized peptides.

110. The multivalent ligand of claim 107 wherein one of SRE¹ or SRE² is an epitope and the other of SRE¹ or SRE² binds to an immune cell.

111. The multivalent ligand of claim 110 wherein the immune cell is a B cell or a T cell.

112. The multivalent ligand of claim 111 wherein one of SRE¹ or SRE² is an epitope recognized as foreign by the B cell or T cell.

113. The multivalent ligand of claim 112 wherein one of SRE¹ or SRE² is an epitope recognized as self by the B cell or T cell.

114. The multivalent ligand of claim 113 wherein one of SRE¹ or SRE² binds to a CR2 receptor on a B cell.

115. The multivalent ligand of claim 114 wherein one of SRE¹ or SRE² binds to a CD22 receptor on a B cell.

116. A complex of a multivalent ligand of claim 96 with one or more proteins wherein in the multivalent ligand the at least one SRE groups binds to the protein.

117. The complex of claim 116 wherein the multivalent ligand comprises a plurality of SRE groups that bind to the protein.

118. The method of claim 116 wherein the protein is a lectin.

119. The complex of claim 118 wherein the SRE groups are monosaccharides.

120. The complex of claim 118 wherein the multivalent ligand is complexed to two or more lectin molecules.

121. The complex of claim 120 wherein the multivalent ligand is complexed to two or more concanavalin A molecules.
- 5 122. A method for enhancing aggregation of biological particles which comprises the steps of:
providing a multivalent ligand which comprises a plurality of recognition elements
which each induce aggregation of one or more of the biological particles and contacting
the biological particles with the complex.
- 10 123. The method of claim 122 wherein the recognition elements are antibodies or lectins.
124. The method of claim 122 wherein the biological particles are cells, viruses or virions.
125. The method of claim 122 wherein the multivalent ligand is a ROMP-derived ligand.
- 15 126. A method for inducing or enhancing induction of apoptosis in a cell which comprises the
steps of:
forming a multivalent ligand which comprises a plurality of signal recognition elements
which bind to the cell and induce apoptosis in the cell and contacting the cells with the
multivalent ligand.
- 20 127. The method of claim 126 wherein one or more of the signal recognition elements is a
lectin.
128. The method of claim 126 wherein the multivalent ligand is a ROMP-derived ligand.
- 25 129. The multivalent ligand of claim 96 which comprises a plurality of two or more different
SRE.
- 30 130. The multivalent ligand of claim 129 wherein the SRE are bonded randomly to the
molecular scaffold.

131. The multivalent ligand of claim 129 wherein the SRE are bonded in a selected pattern to the molecular scaffold.

132. The method of claim 122 wherein the multivalent ligand is bonded to a solid support.

133. A method for generating an assembly of biological macromolecules or particles which comprises the steps of:

(a) providing a multivalent ligand which comprises a molecular scaffold to which a plurality of recognition elements which, in turn, bind to one or more biological macromolecules or biological particles wherein the number, density and spacing of recognition elements bonded to the molecular scaffold are controlled.

(b) contacting the multivalent ligand with biological macromolecules or particles such that the recognition elements of the ligand bind to two or more biological macromolecules or biological particles.

134. The method of claim 133 wherein the biological macromolecules are peptides.

135. The method of claim 133 wherein the biological particles are cells, viruses or virions.

136. The method of claim 133 wherein the multivalent ligand further comprises one or more FE bonded to the molecular scaffold.

137. The method of claim 133 wherein the FE is a detectable label.

138. The method of claim 133 wherein the FE is a group that can be attached to a solid support.

139. The method of claim 133 wherein the molecular scaffold is a polymer.

140. The method of claim 1 wherein the multivalent ligand is bonded to a solid support.

141. The method of claim 82 wherein the multivalent ligand is bonded to a solid support.